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ScienceDirect
Ceramics International 35 (2009) 3389–3393
CERAMICS INTERNATIONAL
www.elsevier.com/locate/ceramint

Potassium-based composition for a bioactive glass

V. Cannillo *, A. Sola

Dipartimento di Ingegneria dei Materiali e dell'Ambiente, Università di Modena e Reggio Emilia, Via Vignolese 905, 41100 Modena (MO), Italy

Received 17 April 2009; received in revised form 9 May 2009; accepted 7 June 2009
Available online 7 July 2009

Abstract

The increasing need for biomedical devices, required to face dysfunctions of natural tissues and organs caused by traumatic events, diseases and simple ageing, has drawn attention onto new materials, that could be able to positively interact with the human body. Among them, Bioglass® is firmly diffused in medical practice, thanks to its high bioactivity. In particular, due to its brittleness, it is mainly applied as a coating onto tougher bionert substrates; nevertheless, its bioactivity may be altered by the crystallization phenomena that could be involved by its processing. With the aim of reducing the tendency to crystallize, a new glass composition, inspired by the 45S5 Bioglass®, was formulated by substituting the sodium oxide with potassium oxide. A parallel characterization of the new glass and the 45S5 Bioglass® was carried out in order to define the effect of the potassium oxide on the thermal behaviour, mechanical properties and bioactivity. The results proved that the thermo-mechanical properties, as well as the *in vitro* response of the two glasses were comparable; however, preliminary tests to produce glass coatings by enamelling evidenced a higher stability of the new glass that, unlike the 45S5 Bioglass®, did not crystallize during processing.

Keywords: B. Microstructure-final; C. Thermal properties; D. Glass; E. Biomedical applications; Enamelling

1. Introduction

Traumatic events and diseases often cause severe damages to the musculoskeletal system; even more, the increasing life expectancy and progressive ageing of population are likely to result in more and more diffused bone tissue disabilities. The standard treatment of bone defects usually requires a surgical operation, with the implant of autologous or allogenic bone grafts. Nevertheless, both of them suffer various disadvantages: autologous bone is often available in very limited amounts, does not always fit the actual application requirements and can be associated with donor site morbidity; allogenic bone, in its turn, can cause immunological intolerances, lack of integration and disease transmission. In order to overcome such difficulties, the development and optimisation of innovative synthetic bone graft substitutes is becoming a urgent need [1].

Potential candidates could be represented by ceramics, such as hydroxyapatite and tri-calcium phosphates, that are able to bond to human bone *in vivo* thanks to their chemical and mineralogical affinity. However, it has been reported that they are not able to bond to soft tissues. So, an interesting alternative is given by bioactive glasses of specific compositions, which show a high bioactivity index and the ability to bond with both hard and soft tissues [2].

In particular, the 45S5 Bioglass® (hereafter named BG-45S5), that was first proposed by Prof. Hench in the 1970 s, has been in clinical use since 1985 [3]. In fact, thanks to its optimal bioactivity, it is widely used in biomedical devices, such as middle ear and dental implants. However, its relatively low strength and brittleness limit its application to non-load-bearing situations [4]. In order to improve the mechanical reliability of glass-based biomedical devices, various approaches have been proposed, such as the production of sintered bodies or the deposition of coatings. However the BG-45S5, like other bioactive glasses, tends to crystallize at high temperature, due to its relatively low content of silica [5]. This is a relevant drawback, since the crystallization is thought to reduce the bioactivity of the glass [6,7] and, on the other hand, thermal treatments are widely required to obtain not only special products, such as sintered glass scaffolds or glass fibres, but also ordinary coatings [5]. It has been proved that the crystallization tendency of bioactive glasses (made of sodium oxide, lime, phosphorous pentoxide and silica) may be significantly reduced by adding proper oxides, such as potassium oxide, to their composition [5].

* Corresponding author. Tel.: +39 059 2056240; fax: +39 059 2056243.
E-mail address: valeria.cannillo@unimo.it (V. Cannillo).

0272-8842/$36.00
doi:10.1016/j.ceramint.2009.06.011

Therefore, in the present research, a new glass, named BioK, was derived from the BG-45S5 by substituting all the sodium oxide with potassium oxide and the effect of the compositional change on the thermo-mechanical properties and the bioactivity was evaluated. Moreover, with the aim of directly testing the effect of potassium oxide on the manufacturing of glass coatings, both glasses were used to glaze bulk alumina substrates by enamelling. The complete substitution of sodium oxide with potassium oxide was expected to emphasize the effect of the new formulation on the glass behaviour.

2. Experimental

As mentioned before, the composition of the BioK was inspired by that of the BG-45S5 [8], but all the sodium oxide was substituted with potassium oxide. Hence the BioK composition resulted: SiO_2: 46.1 mol%; P_2O_5: 2.6 mol%; CaO: 26.9 mol%; K_2O (which substituted the Na_2O): 24.4 mol%. In order to melt the glasses, reagent grade SiO_2, $CaCO_3$, $Na_3PO_4{\cdot}12H_2O$ or $K_3PO_4{\cdot}H_2O$ (for BG-45S5 or BioK, respectively), and Na_2CO_3 or K_2CO_3 (for BG-45S5 or BioK, respectively) were used (commercial powders by Carlo Erba Reagenti, Italy). The proper raw materials for each sample were weighted, mixed in a polymer flask and melted in a platinum crucible. The same thermal cycle was set for the two glasses: from room temperature to 1100 °C at 10 °C/min; at 1100 °C for 1 h; from 1100 °C to 1450 °C at 10 °C/min; at 1450 °C for 30 min. After that, for each glass, the melt was rapidly quenched in water (at room temperature), dried overnight in a furnace at 110 °C, ground in an agate jar and sieved to obtain <75 μm particles. Alternatively, in order to obtain glass bulks for further characterization purposes (e.g. thermodilatometric tests), the melt was poured in a graphite mould, annealed at 550 °C for 1 h and left to cool down slowly overnight inside the furnace.

The glass powders and bulks underwent an X-ray diffraction, XRD (PANalytical X'pert PRO), to check that no crystallization had occurred due to the introduction of the potassium oxide.

The coefficient of thermal expansion of the two glasses was measured on 5 mm × 5 mm × 15 mm bulk samples by an optical dilatometer (Misura 3.32, Expert System Solutions), working in the 50–500 °C temperature range, with a heating rate of 10 °C/min.

For each glass, after mounting a sample in resin and polishing, the micro-hardness was tested via Vickers indentation, applying a 25 g_f load for 15 s (Wolpert Group, Micro-Vickers Hardness Tester digital auto turret, Mod. 402MVD); at least 10 valid indentations (no evident cracks or other defects) were considered to calculate a mean value [9]. The micro-indentation test was used to evaluate also the toughness; with this aim, the applied load was set to 100 g_f and the toughness was derived from the length of the diagonals of the indents and the cracks according to Evans and Charles equation [10]. Again, at least 10 indentations were taken into consideration. To facilitate the measurements, SEM images of the indents were acquired (ESEM Quanta 2000).

Moreover, in order to determine the local elastic modulus, a depth-sensing Vickers micro-indentation experiment was performed on a mounted and polished sample of each glass (OpenPlatform, CSM, Switzerland); the maximum load of 50 g_f was applied for 15 s, the load–depth curve was recorded and the elastic modulus was calculated according to the Oliver and Pharr method [11]. Again 10 indentations were considered to obtain a mean value.

The bioactivity was investigated by immersion in simulated body fluid (SBF) [12]; for each glass, the samples were extracted after 1, 2 and 4 weeks and analysed by XRD and SEM (operated in low vacuum – pressure: 0.5 Torr), coupled with X-ray energy dispersion spectroscopy, X-EDS (Oxford INCA-350).

Glass coatings were deposited by enamelling on commercial polycrystalline alumina substrates (Keramo Ceramiche Tecniche, Tavernerio, Como, Italy); for each composition, a thin slice of glass (no thicker than 1 mm) was placed on top of an alumina substrate and heat treated from room temperature to 500 °C at 5 °C/min and then from 500 °C to 1400 °C at 10 °C/min, left at 1400 °C for 4 h and carefully extracted from the furnace.

3. Results and discussion

The bulk samples of both glasses appeared transparent and homogeneous.

The absence of any relevant crystallization caused by the introduction of the potassium oxide was confirmed by the XRD, since the spectra of both glasses, in bulk and in powder form, showed the typical trend of amorphous phases (no sharp peaks were detected). As an example, Fig. 1 presents the spectra taken from the bulk glasses (together with those of the samples immersed in SBF).

The coefficient of thermal expansion of the BioK was very similar to that of the BG-45S5, since they resulted to be $13.8 \times 10^{-6}\,K^{-1}$ and $12.7 \times 10^{-6}\,K^{-1}$, respectively. It is known from the literature that, in binary alkali–silicate glasses, at the same concentration the potassium-modified silicate glass has a higher expansivity than the sodium-modified silicate glass [13]. Even if, in the present research, both the BioK and the BG-45S5 were not binary glasses, it is reasonable that the substitution of the sodium oxide with potassium oxide similarly resulted in a slight increase of the coefficient of thermal expansion. However it is worth noting that the change induced by the compositional modification was not substantial.

Moreover it is interesting to observe that the introduction of the potassium oxide did not alter the mechanical properties of the glass, in spite of the fact that the field strength of K^+ is lower than that of Na^+. This result can be appreciated from the comparison between the mechanical properties of the two glasses presented in Table 1. The values of the Vickers hardness and fracture toughness of the BG-45S5 seem to be lower than the values usually reported in the literature [2,14], probably due to the operator-dependence of the indent and crack measurements; however, in the present research, all the evaluations were performed strictly following the same procedure, in order

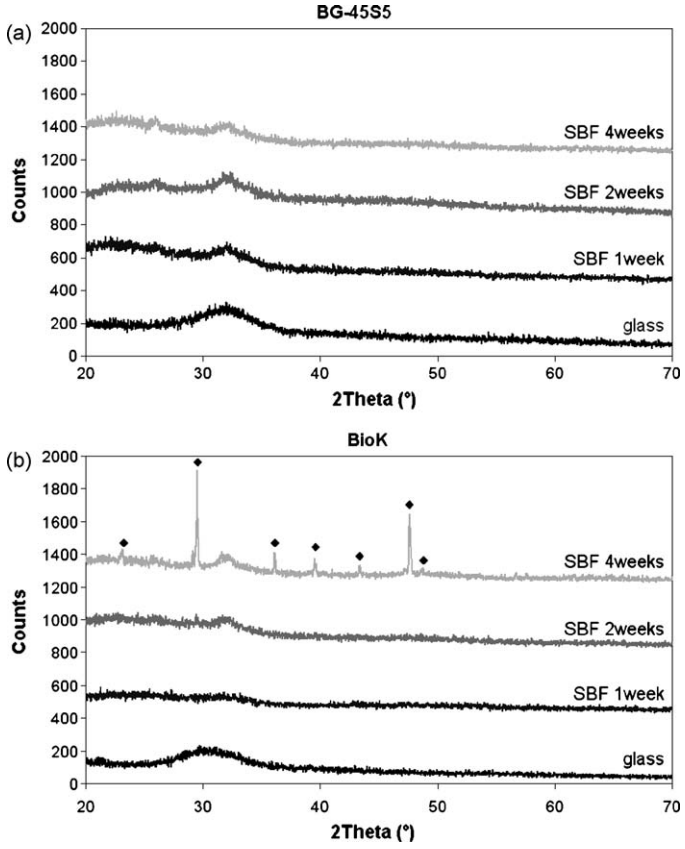

Fig. 1. XRD spectra of the BG-45S5 (a) and BioK (b) glasses. For both compositions, a comparison between the initial glass and the samples immersed in SBF is proposed. (◆): Calcium carbonate (JCPDS-ICDD 00-05-0586).

Table 1
Comparison between the mechanical properties of the BG-45S5 and the BioK glasses.

	Vickers hardness (GPa)		Toughness (MPa $m^{1/2}$)		Young's modulus (GPa)	
	Mean	Std. dev.	Mean	Std. dev.	Mean	Std. dev.
BG-45S5	2.50	0.46	0.30	0.03	83.4	1.7
BioK	2.54	0.44	0.32	0.02	84.2	1.1

to have a meaningful comparison between the properties of the two glasses. The value of the elastic modulus, instead, is somewhat higher than that available in the literature [2,14]. Such discrepancy is ascribable to the experimental method, since the depth-sensing indentation gives a local value of the elastic properties; moreover, the non-clearly readable indents, usually located on local defects, are generally disregarded and therefore the so-obtained values of the elastic properties are representative of a defect-free material. However, also in this case, the procedure adopted for the two glasses was the same, in order to have comparable data.

As regards the *in vitro* tests, the XRD spectra acquired on the immersed samples are reported in Fig. 1. The presence of calcium carbonate (00-05-0586) was detected on the BioK sample extracted after 4 weeks. However, it is plausible that the calcium carbonate was simply originated by a precipitation from the SBF, since this is a common phenomenon in *in vitro* tests in SBF [12]; moreover, the SEM inspection revealed large and well developed calcium carbonate crystals, which looked extraneous from the glass surface, corroborating the hypothesis of a precipitation from the SBF. Apart from the calcium carbonate, no sharp peaks were observed. However, for both glasses, extending the immersion time the glass "hump" progressively decreased (in width), a broad signal appeared in the 30–33° 2θ range, where the main peaks of hydroxyapatite are located [15], and it was associated with an amorphous "halo" at about 20–25°. It is interesting to observe that the BioK behaviour was strikingly similar to that observed for a glass belonging to the SiO_2–CaO–K_2O system investigated by Vitale Brovarone et al. [16]. In fact, the XRD pattern of the as-produced glass showed a broad "hump" centred on about $2\theta = 30°$, confirming the amorphous nature of the starting material [16]. After 1 week of immersion in SBF, the diffraction pattern of the glass studied by Vitale Brovarone et al. exhibited a broad signal at about 31–32° and an amorphous halo a few degree lower; the broad shape of the peaks at 31–32° was caused by the microcrystalline nature of the growing hydroxyapatite while the amorphous halo, shifted to lower diffraction angles with respect to the initial "hump", was traced back to the formation of a silica gel layer on the glass surface [16]. Sharper and more defined hydroxyapatite peaks were found after 3 months in SBF, thanks to the wider development of hydroxyapatite [16].

The SEM observation revealed that, after 4 weeks of immersion, globular features could be seen on the samples of both BG-45S5 and BioK; they strictly resembled the "cauliflower-like" structures frequently observed on bioactive materials after immersion in SBF and usually identified as newly formed hydroxyapatite [17]. A representative image, acquired on the BioK sample immersed for 4 weeks, is reported in Fig. 2.

As regards the Ca/P ratio, which is 1.67 in pure hydroxyapatite [15], its value for the BG-45S5 changed from 1.39 after 1 week to

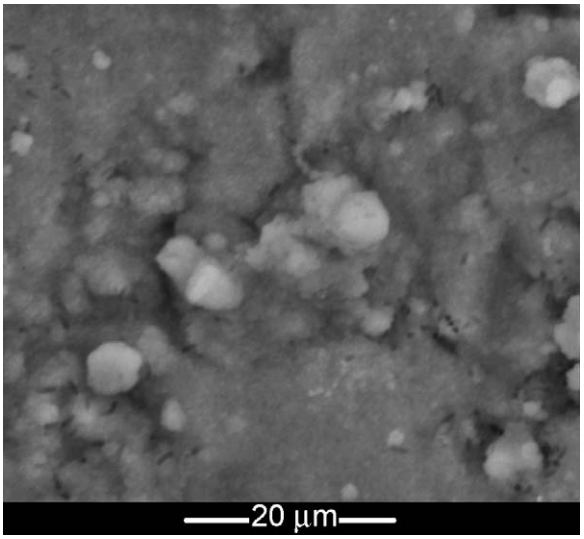

Fig. 2. Globular features on the surface of the BioK sample immersed for 4 weeks.

1.45 after 2 weeks and to 1.75 after 4 weeks, oscillating around the theoretical value. Instead, the value of the Ca/P ratio for the BioK went from 1.58 after 1 week to 1.46 after 2 weeks and passed to 2.00 after 4 weeks. The last measure, however, was influenced by the presence of calcium carbonate precipitated from the SBF; that could justify the unusually high value observed. Hence the combined results of XRD, SEM and X-EDS suggest that a hydroxyapatite layer is growing on the surface of the glasses, on both the BG-45S5 and the BioK, confirming the bioactivity of the new potassium-based glass.

Since the mechanical properties of glasses, especially their brittleness, prevent their application in load-bearing service conditions, bioactive glasses are mainly used as coatings on tougher substrates, such as alumina. The enamelling is a cost- and time-effective technique to obtain glass coatings [18], however it requires a heat treatment which could promote a crystallization of the bioactive glass. In the present research, a first attempt to deposit a glass layer by enamelling was carried out using a thin glass slice.

In Fig. 3, the cross-section of the two glazed samples (with BG-45S5 and with BioK) is presented. In both cases, there was not a sharp interface between the glass coating and the alumina substrate, since the glass gradually penetrated into the alumina bulk (graded area in Fig. 3) [19].

Even if the coatings resulted flat and well adhered for both glasses, the XRD performed on the surface revealed that the BG-45S5 underwent a partial crystallization, with the development of a calcium silicate (00-046-0044), while the BioK remained perfectly amorphous (all the peaks in the corresponding XRD spectrum were caused by the alumina of the substrate, 01-071-1125, rising to the surface). The comparison between the XRD spectra is shown in Fig. 4.

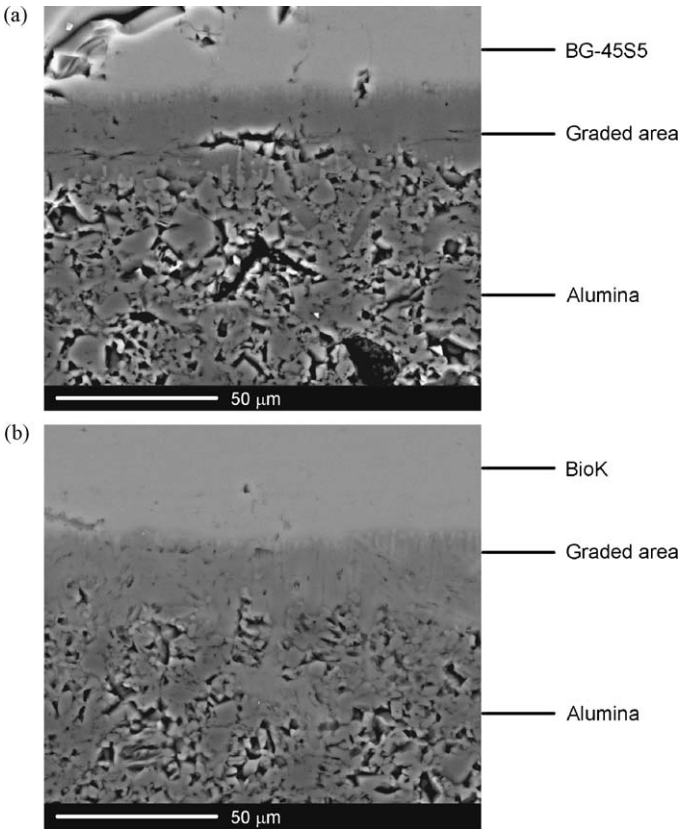

Fig. 3. Cross-section of the glass coatings on alumina substrates obtained via enamelling: (a) BG-45S5 coating and (b) BioK coating.

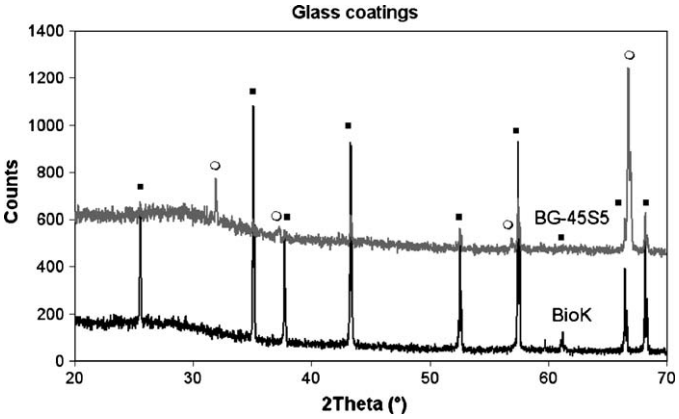

Fig. 4. XRD spectra of the coatings produced via enamelling using the BG-45S5 and BioK glasses. (○): Calcium carbonate (00-046-0044) and (■): alumina (01-071-1125).

This is an encouraging result, since a crystallization process could reduce the bioactivity of the glass [6]. As a matter of fact, the consequence of the crystallization on the bioactivity of the BG-45S5 is still under debate, since the bioactivity is affected by several features such as the specific crystalline phases developed during the heat treatment and the size of the newly formed crystals [20]. However it is generally thought that a reduction in amorphous phase content could limit the reactivity of bioglasses [7]. So, the limited tendency shown by the BioK to crystallize at high temperature could facilitate its usage to manufacture high performance biomedical devices.

4. Conclusions

A new glass composition was derived from the BG-45S5 by substituting the sodium oxide with potassium oxide, which is thought to reduce the BG-45S5 tendency to crystallize. The characterization proved that the thermo-mechanical properties were not altered by the introduction of the potassium oxide; most of all, the bioactivity of the glass was preserved. However the potassium-containing glass turned out to be more suitable than the BG-45S5 for manufacturing a glass coating by enamelling, since it did not crystallize during the heat treatment thanks to the potassium.

Even if further investigation is required (for example, in order to analyse various compositions containing both sodium and potassium oxides; to evaluate the applicability of the glasses in different fabrication processes; to assess the bioactivity of the coatings) the presence of potassium oxide seems to help the usage of these bioactive glasses, without damaging their thermo-mechanical performances and their bioactivity.

Acknowledgement

Mr. Andrea Milanti is gratefully acknowledged for his precious help to prepare and characterize the glasses.

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